REMARKS

Reconsideration and withdrawal of the rejections of and objections to the claims are respectfully requested in view of the amendments and remarks which follow.

Claims 1-63 were pending in this application. Claims 3, 4, 33, 38-45, 47 and 49-63 are cancelled without prejudice and disclaimer. Claims 1, 14, 46 and 48 are amended to more clearly define and particularly point out the claimed invention. New claims 64-67 are added by this amendment. Support for the above amendments can be found in the specification and claims as originally filed. More specifically, support for the new claims 64-67 can be found in the specification on pages 6 through 9. No new matter is added by this amendment. Accordingly, claims 1, 2, 5-32, 34-37, 46, 48, and 64-67 are pending in this application.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance.

I. Restriction Requirement

The Examiner imposed the following restriction requirement under 35 U.S.C. § 121:

Group I: Claims 1-3, 5-63, drawn to the compounds of formula I wherein m=n=p=0, q=1, their compositions and one method of use, classified in class 546, subclass 118;

Group II: Claims 1, 2, 4-63, drawn to a compound of the formula I wherein n=p=0, m=q=1, their compositions and one method of use, classified in class 540, subclass 578; and

Group III: Claim 1-63, drawn to a compound, compositions, and methods of use not included in Group I, classified in classes and subclasses depending on the nature of the substituents.

During a telephone conversation with the Examiner on April 20, 2001, Reza Green provisionally elected, with traverse, to prosecute the invention of Group I (claims 1-3, 5-44, along with claims 46 and 48). Applicants hereby affirm the verbal election of the claims of Group I for further prosecution in this application.

Applicants respectfully submit that the claims of Groups I, II and III should not be subject to restriction as all of the claims are directed to a single inventive concept, i.e., a novel class of

substituted imidazole compounds, pharmaceutical compositions containing them and their use in the treatment of diseases and disorders related to the histamine H3 receptor, and that these Groups of claims may be examined together in one application without undue burden on the Examiner.

Nonetheless, in order to be fully responsive and advance prosecution of this application, Applicants have cancelled the non-elected subject matter and expressly reserve the right to file divisional or continuation applications directed to the non-elected and/or cancelled subject matter.

II. The Rejection of Claims 1, 2, 5-44, 46, and 48 - Improper Markush Grouping

Claims 1, 2, 5-44, 46, and 48 were rejected under the judicially created doctrine as being an improper Markush grouping. The Examiner indicated that the deletion of non-elected subject matter would overcome this rejection. (Office Action, page 4)

In response to this rejection, the claims have been amended to reflect that the compounds of the elected invention are directed to compounds of formula I wherein m=n=p=0, and q=1. Accordingly, Applicants submit that the amended claims overcome this rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

III. Priority Documents

The Examiner is thanked for aknowledging the claim for foreign priority in this applciation. It was noted in the Office Action that the certified copies of the priority documents as required by 35 U.S.C. 119(b) have not been filed in this application.

It is respectfully noted that the certified copies of the priority documents, namely, Danish patent appalication nos. PA 1999 00508, PA 1999 01345 and PA 2000 00042 filed on April 16, 1999, September 22, 1999 and January 12, 2000, respectively, are attached to this response. Accordingly, the requirements of 35 U.S.C. 119(b) are fulfilled.

IV. Rejection of Claims 1-3, 5-44, 46, and 48 under 35 U.S.C. § 112, first paragraph

Claims 1-3, 5-44, 46, and 48 were rejected under 35 U.S.C. § 112, first paragraph, because: (a) the specification allegedly has no definition for the terms heteroarylamino, heteroaryl, heteroaroyl; (b) the specification allegedly does not provide sufficient guidance for the variable groups, such as X, Y, A, and R's, in preparing additional H3 receptor antagonists on the

imidazo[4,5-d]pyridine ring system; and (c) the scope of a functional group which can be converted to hydrogen *in vivo* is allegedly not adequately enabled by the specification. These rejections are respectfully traversed.

(a) Rejection based on the terms "heteroaryl, heteroaroyl, heteroarylamino"

Claims 1-3, 5-44, 46, and 48 were rejected under 35 U.S.C. § 112, first paragraph, due to the terms "heteroaryl, heteroaroyl, and heteroarylamino" because the specification allegedly has no specific definition for these terms, except some examples.[1] (Office Action, page 5).

It is respectfully asserted that the specification supports the full scope of the invention as claimed, fully enables the pending claims, and provides sufficient guidance and direction for one skilled in the art to make and use the invention as claimed. Contrary to the Examiner's assertion, the specification does contain specific definitions for the heteroaryl, heteroaroyl, and heteroarylamino terms. (See e.g.: page 6, line 21 to page 7, line 5; page 7, lines 7 to 10; and page 7, lines 16 to 20; respectively.) The definitions in the specification also include numerous examples of various types of heteroaryl, heteroaroyl and heteroarylamino groups.

The claims have been amended herein such that the definitions for these groups are now included in the claims. For example, amended claim 1 includes the following language:

> "heteroaryl is a 3 to 7 membered monocyclic or a 9 to 14 membered bi- or tricyclic aromatic system containing one or more heteroatoms selected from N, O or S, which is optionally partially or fully hydrogenated; heteroarylamino is a radical wherein a -(NH)- group is linked to a heteroaryl group; heteroaroyl is a radical wherein a -(C=O)- group is linked to a heteroaryl group."

Accordingly, the pending claims include a description of the nature and type of groups encompassed by the heteroaryl, heteroaroyl, and heteroarylamino terms, and are fully supported and described in the specification.

In addition, new claims 65-67 are added. These new claims, which are dependent on claim 1, are directed to the specific heteroaryl (claim 65), heteroaroyl (claim 66), and

[1] These claims were also rejected under the second paragraph of 35 U.S.C. § 112 based on the "heteroaryl and heteraroyl" terms. (Office Action, page 7).

heteroarylamino (claim 67) groups specifically exemplified in the specification on pages 6 through 9. Accordingly, the pending claims are adequately enabled by the specification.

These definitions have been added to merely clarify that terms as originally used in the claims and these amendments are not an indication of the surrender of any subject matter. These amendments are made in an earnest effort to advance prosecution of this application and are made without any intention of creating estoppel with respect to equivalents.

Applicants respectfully assert that one skilled in the art could practice the full scope of the invention as claimed for the variety of possible heterocyclic radicals based on the guidance and direction in the specification and the knowledge in the art. The terms used to describe the claimed invention are used in their conventional sense and in the way one skilled in the art would use these terms, and these terms clearly define the nature and type of heterocyclic groups claimed. The Examiner has presented no evidence as to why the use of these terms is not commensurate with the scope of protection the Applicants are entitled to.

For the foregoing reasons, Applicants submit that the specification fully supports the amended claims and fulfills the requirements of the first paragraph of 35 U.S.C. § 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

(b) Rejection based on the variable groups on the imidazo[4,5-d]pyridine ring system

Claims 1-3, 5-44, 46 and 48 were rejected under 35 U.S.C. § 112, first paragraph, because the specification is allegedly not enabled for the full scope of the compounds as claimed. According to the Office Action, the specification discloses many compounds but there is allegedly insufficient guidance in preparing additional H3 receptor antagonists and that only those compounds wherein R^5 and R^6 are hydrogen, A is a bond, R^3 or R^4 is hydrogen, methyl, alkyl-substituted phenyl, spiro, alkyl of the claimed invention have been made. (Office Action, page 5).

It is respectfully asserted that the specification fully enables one skilled in the art to practice the full scope of the claimed invention. The specification fully describes the various types of functional groups that can be used for the various X, Y, A, Z and R's in the different positions of the compounds of formula I. The specification defines these functional groups, including representative example for each of these groups, on pages 4 through 9. For example, the term C_{1-6}-alkyl is defined as a branched or straight hydrocarbon group having from 1 to 6

carbon atoms, and includes a discussion of typical C_{1-6}-alkyl groups as including, but not limited to, methyl, ethyl, n-propyl, isopropyl, butyl, isobutyl, *sec*-butyl, *tert*-butyl, pentyl, isopentyl, hexyl, isohexyl, and the like. (Specification, page 4) No special definitions are included in the specification and all terms are defined in such a way that they have their conventional meaning as used by one of ordinary skill in the chemical arts.

Further, the specification includes numerous synthesis examples on pages 67 to 134, including both generic and specific chemical pathways. General synthesis schemes for starting materials are included in the specification on pages 67 to 72. Other intermediate compounds and building blocks are discussed on pages 73 to 76, including a further generic parallel synthesis pathway disclosed on pages 84 to 85. These starting materials, intermediates and chemical pathways provide clear guidance to one skilled in the art, such that the skilled practitioner can make and use the full scope of the invention as claimed, by simply making the required substitutions for the X, Y, A, Z and R groups as described in the claims and specification. These starting and intermediate compounds are then used in the disclosed synthetic methods to produce the numerous compounds in the examples which follow on pages 76 to 134.

Further, one skilled in the art could easily follow the General Procedure A on pages 69 to 70, and produce compounds wherein R^3, R^4, R^5, R^6, and A are other than groups described by the Examiner. The general scheme discloses reaction conditions, reagents and solvents, and process steps, including alternative purification methods, which could easily be adapted by one skilled in the art without undue experimentation to make a variety of compounds covering the full scope of the claimed invention based on the guidance provided in the specification and the practitioner's knowledge of the chemical arts.

The specification also includes guidance as to how one skilled in the art would test the compounds made by following the instructions provided in the specification. On pages 135 to 137 of the specification, guidance is provided as to how one skilled in the art would test the ability of the compounds produced to interact with the H3 receptor. Detailed instructions as to alternative binding assays for testing these compounds are provided. The binding assay procedures described in the specification include the materials required for performing the assays (source materials, buffers, reagents, filters, etc.), testing steps and conditions, suggested equipment, and a discussion of the analysis of the test results.

Thus, the full scope of the pending claims are supported by the specification, in combination with the knowledge of one skilled in the art, such that sufficient guidance and direction are provided and no undue experimentation is needed to practice the full scope of the invention as claimed.

The Examiner's attention is respectfully invited to some case law under the first paragraph of Section 112. First, it is a well-known principle that claims must be read in light of the specification. In re Marosi, 710 F2d 799, 218 USPQ 289 (Fed. Cir. 1983). The first paragraph of Section 112 requires nothing more than objective enablement. How this is accomplished is of no importance. In re Marzocchi, 169 USPQ 367 (CCPA 1971). Second, it has been determined that the claims need not be limited to preferred embodiments in the specification. It is improper, according to In re Goffe, 191 USPQ 429, 431 (CCPA 1976), to limit the claims of an application to the specific examples in the specification under the guise of lack of enablement:

> To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for 'preferred' materials...would not serve the constitutional purpose of promoting progress in the useful art.

Third, it is urged that the subject matter in the claims is not broader than the enabling disclosure. Applicants respectfully submit that the claims are more than adequately supported by the specification. There is no particular number of examples which makes specific claim language adequate or enabled. Indeed, enablement is not even related to the number of examples in the specification. In In re Borkowski, 164 USPQ 642, 646 (CCPA 1972), the Court stated:

> There is no magical relation between the number of representative examples and the breadth of the claims...the number and variety of examples are irrelevant if the disclosure is 'enabling' and sets forth the best mode contemplated.

In addition, it is respectfully urged that enablement is not precluded even if some experimentation is necessary, provided it is not unduly extensive. Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986). A disclosure is enabling even if considerable amounts of experimentation is involved, if that experimentation is routine. Ex parte Forman, 230 USPQ 546, 547 (BPAI 1986). In Ex parte Forman, the Board described what constituted undue experimentation as follows:

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experiment should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. The factors considered have been summarized as the quantity of experimentation necessary, the amount of direction and guidance presented, the presence or absence or working examples, the nature of the invention, the relative skill of those in the art, the predictability and unpredictability of the art and the breadth of the claims.

It is respectfully submitted that any experimentation required by the present application is routine, and that sufficient guidance and direction for this experimentation is provided in the specification. Only routine experimentation related to chemical synthesis or biological testing disclosed in the specification or known in the art would be required to make and use the full scope of the invention as claimed.

In view of the foregoing, it is respectfully submitted that the teaching in the application, in combination with the knowledge of one skilled in the art, fully enables one skilled in the art to make and use the full scope of the claimed invention without undue experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

(c) Rejection based on the use of the "functional group which can be converted to hydrogen *in vivo*" language

Claim 1 was rejected under 35 U.S.C. § 112, first paragraph. According to the Office Action, the specification allegedly does not provide enablement for the scope of R^1 equal to all possible functional groups which can be converted to hydrogen *in vivo*.

Contrary to the Examiner's assertion, the specification provides enablement for R^1 in formula I for a variety of functional groups that can be converted to hydrogen *in vivo*. For example, various groups are specifically exemplified in the specification on page 8, line 30 to

page 9, line 6. The specification clearly indicates these groups are merely representative of groups which can be converted to hydrogen *in vivo* and are intended to be "non-limiting examples" of such groups. The applicants' intent is clearly to include any group for further substitution of R^1 which upon administrating the presently claimed compounds can be converted to hydrogen, either enzymatically or by the acidic environment of the stomach. One skilled in the art would know and clearly recognize that other groups could be converted to hydrogen *in vivo*. Further, it would not require undue experimentation for one skilled in the art to ascertain what functional groups can be converted to hydrogen *in vivo*, as the determination and elucidation of metabolites is part of the routine pharmacological and pharmacokinetic testing performed on these types of compounds.

As discussed above, it is not proper to limit the claims to the specific examples or embodiments disclosed under the guise of lack of enablement, if the broader definition of the invention claimed would be clear to one skilled in the art. In fact, the limitation "a group which can be converted into (X) *in vivo*" by itself, without further definition or limitation of the term "group" in the claim(s), has been recognized by the U.S. Patent and Trademark Office (PTO). The Examiner's attention is respectfully directed, *inter alia*, to the following issued U.S. Patents: 6,121,308; 6,057,324; 5,637,598; 5,541,229; 5,494,914; 5,446,071; 5,270,322; and 5,250,541.

For example, claim 1 of U.S. Patent No. 6,057,324 includes the following limitations: "R^1: a group which can be converted into an amidino group *in vivo*" and "R^2 and R^3: the same or different and each represent a carboxyl group or a group which can be converted into a carboxyl group *in vivo*." (Emphasis added) No further definition of the "group" is provided in the claim 1. Similarly, claim 1 of U.S. Patent No. 5,637,598 includes the following limitation: "R^5 and R^6 each are independently hydrogen, hydroxy, or a moiety which is converted to hydroxy *in vivo*;" without further definition of the "moiety" in the claims.

Given the inventive concept encompassed by the present claims and disclosed in the specification, and the fact that the objected to limitation is recognized in the art, those of ordinary skill in the art would be able to practice the full scope of the claimed invention without undue experimentation. Nonetheless, in an effort to advance prosecution of this application, new claim 64 has been added. New claim 64 adds a further limitation to the R^1 radical of the compounds of formula I in claim 1. New claim 64 includes in the definition of R^1, the groups specifically

exemplified in the specification on pages 8 and 9 of the specification, and therefore are clearly enabled by the specification.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under the first paragraph of 35 U.S.C. § 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. Rejection of Claims 1-3, 5-44, 46, and 48 under 35 U.S.C. § 112, second paragraph

Claims 1-3, 5-44, 46, and 48 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for the following reasons: (a) the use of heteroaryl and heteroaroyl in the definition of R variables is unclear; (b) claim 1 is vague for the use of "as well as"; (c) claim 14 is not dependent on a preceding claim; and (d) the use of "medicament" claims does not comply with normal US claim format. For the reasons which follow, these rejections are respectfully traversed.

The claims have been amended in response to these rejections. With respect to the rejection of the claims under the second paragraph of 35 U.S.C. § 112 due to the "heteroaryl and heteroaroyl" terms, it is respectfully asserted that these terms are definite and provide a clear meaning to one skilled in the art. However, to be fully responsive to the Office Action and in an effort to advance prosecution of this application, the claims are amended to include definitions for the heteroaryl and heteroaroyl terms. These definitions include a description of the size and type of the heterocyclic systems included by the terms, and include that the heteroatoms must be selected from the group consisting of nitrogen, oxygen and sulfur. It is respectfully asserted that the terms heteroaryl and heteroaroyl are not indefinite and clearly define and particularly point out the subject matter of the claimed invention. In view of these amendments and the discussion of the rejection of the claims under 35 U.S.C. § 112, first and second paragraph, based on the heteroaryl and heteroaroyl terms above, reconsideration and withdrawal of this rejection is respectfully requested.

With respect to (b) above, claim 1 has been amended as suggested by the Examiner in the Office Action. With respect to (c) above, claim 14 has been amended to properly be dependent on claim 12. Lastly, claims 33, and 38-40 have been cancelled by this amendment. Accordingly, (d) of the rejection above is rendered moot by the removal of the "medicament" claims.

For the foregoing reasons, Applicants submit that the amended claims overcome the rejections under 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. The Rejection of Claims 1-3, 5, 7-11, 20, 33-44, 46, and 48 under 35 U.S.C. § 102

Claims 1-3, 5, 7-11, 20, 33-44, 46, and 48 are rejected under 35 U.S.C. § 102 for allegedly being anticipated by the following references: (a) Remelli et al., Chem Abstract 128:75655; (b) Krause et al., J. Med Chem., 1995; (c) Arcari et al., DE 2700012; (d) Hauck et al., Chem Abstract 92:146611; (e) Yutilov et al., Chem Abstract 99:70725; (f) Scarponi et al., GB 2158440; (g) Stocker et al., Chem Abstract 112:216653; (h) Klutchko et al., Chem Abstract 114:229317; (i) Vincent et al., Chem Abstract 117:251781; (j) Clarke et al., WO 92/18115; (k) Enari et al., EP 589665; (l) Suzuki et al., Chem Abstract 126:104085; (m) Thorwart et al., Chem Abstract 127:65701; and (n) Casella et al., J. Am. Chem Soc. 103, pp. 6338-6347 (1981). These rejection are respectfully traversed.

It is respectfully asserted that none of the compounds disclosed in any of the prior art references cited in the Office Action are encompassed by the pending claims. For example, the compound disclosed by (a) Remelli et al., namely 5-methyl-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridine, is specifically excluded from the claims based on the limitation "when $R^1=R^2=R^3=R^4=R^5=R^6=$hydrogen, -X-Y-A-Z must not be methyl."

Similarly, the compounds disclosed by (b) Krause et al., for example, the specific 4-phenyl-6-methyl-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridines, are not encompassed by the amended claims. The compounds disclosed in Krause correspond to compounds wherein -X-Y-A-Z of formula I would be hydrogen, which are not included in the amended claims.

Further, the compounds disclosed by: (c) Arcari et al. (DE 2700012) are not encompassed by the amended claims, because the compounds disclosed in Arcari correspond to compounds wherein -Y-A-Z in formula I of the amended claims must be $-NH_2$, optionally substituted with ethyl or isopropyl, which are not included in the pending claims;

(d) Hauck et al. (Chem Abstract 92:146611) are not encompassed by the amended claims, because the compounds disclosed in Hauck correspond to compounds wherein -X-Y-A- of

formula I of the amended claims must be $-CH_2CH(OH)CH_2-$, which are not included in the pending claims;

(e) Yutilov et al. (Chem Abstract 99:70725) are not encompassed by the amended claims because the compounds disclosed in Yutilov correspond to compounds wherein -X-Y-A- of formula I of the amended claims must be $-CH_2CH(OH)-$, which are not included in the pending claims;

(f) Scarponi et al. (GB 2158440) are specifically excluded from the claims based on the limitation "when $R^1=R^2=R^3=R^4=$hydrogen, C_{1-4}-alkyl, C_{2-4}-alkeny or phenyl, or $R^2=R^3=R^4=C_{3-7}$-cycloalkyl, $R^6=$hydrogen, and XYAZ begins with -C(=O)-, -C(=O)-O-, -C(=O)-NH- or -C(=S)-NH-, R^5 must not be $-C(=O)-NH_2$, which is optionally substituted with C_{1-4}-alkyl, C_{2-4}-alkenyl, C_{3-7}-cycloalkyl, or phenyl";

(g) Stocker et al. (Chem Abstract 112:216653) are specifically excluded from the claims based on the limitation "when $R^1=R^2=R^4=R^5=R^6=$hydrogen, R^3 = 4-methylphenyl, 4-methoxyphenyl or 4-chlorophenyl, -X-Y-A-Z must not be methyl, $-CH_2$-phenyl or benzoyl";

(h) Klutchko et al. (Chem Abstract 114:229317) and (i) Vincent et al. (Chem Abstract 117:251781) are specifically excluded from the claims based on the limitation "when -X is -CO-, the group -Y-A-Z starts with the radical -CH<, $R^1=R^2=R^3=R^4=R^6=$hydrogen, R^5 must not be hydroxymethyl, C_{1-6}-alkoxycarbonyl or carboxy";

(j) Clarke et al. (WO 92/18115) are not encompassed by the amended claims because the compounds disclosed in Clarke correspond to compounds wherein R^3 of formula I of the amended claims must be pyrrolidine, which are not included in the pending claims;

(k) Enari et al. (EP 589665) are specifically excluded from the claims based on the limitation "when -X is -CO-, the group -Y-A-Z starts with the radical -CH<, $R^1=R^2=R^3=R^4=R^6=$ hydrogen, R^5 must not be hydroxymethyl, C_{1-6}-alkoxycarbonyl or carboxy";

(l) Suzuki et al. (Chem Abstract 126:104085) are specifically excluded from the claims based on the limitation "when $R^1=R^2=R^3=R^4=R^5=R^6=$hydrogen, -X-Y-A-Z must not be 2-methoxy-4-amino-5-chloro benzoyl";

(m) Thorwart et al. (Chem Abstract 127:65701) are specifically excluded from the claims based on the limitation "when $R^1=R^2=R^3=R^4=R^5$=hydrogen, R^6=carboxy, -X-Y-A-Z must not be (4-methoxyphenyl)sulfonyl"; and

(n) Casella et al. (J. Am. Chem Soc. 103, pp. 6338-6347 (1981)) are not encompassed by the amended claims, because the compounds disclosed in Casella correspond to compounds wherein -X-Y-A-Z of formula I would be hydrogen, which are not included in the amended claims.

Therefore, since the amended claims do not encompass any of the compounds disclosed by the cited references, the claims cannot be anticipated by the references.

It is respectfully submitted that the amended claims overcome these rejections under 35 U.S.C. § 102. Applicants respectfully request reconsideration and withdrawal of these rejections.

VII. Rejection of Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32 and 33-37 under 35 U.S.C. § 103

Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32, and 33-37 were rejected under 35 U.S.C. § 103 as allegedly being unpatentable in view of Arcari et al, DE 2700012. Specifically, the Office Action states that the claimed invention differs from the reference by reciting a specific species and/or a more limited genus than the reference, and that it would have been obvious to one skilled in the art to be motivated to select any of the species of the genus taught by the reference because the skilled chemist would have a reasonable expectation that any species selected would have similar properties as the same use as taught for the genus as a whole. (Office Action, page 12). This rejection is respectfully traversed.

Applicants respectfully assert that the present invention is not rendered obvious by the cited reference. As discussed above with respect to the 35 U.S.C. § 102 rejection based on the Arcari reference, the amended claims do not encompass any of the compounds disclosed in Arcari. Contrary to the Examiner's statement, it is respectfully asserted that the compounds encompassed by the amended claims are not specific species included in the generic scope of the compounds taught in the Arcari reference.

Further, the Arcari reference does not include any suggestion or motivation to one skilled in the art to modify the compounds disclosed therein, to make and use the presently claimed

compounds.[2] Arcari discloses a generic group of 4,5,6,7-tetrahydroimidazo-[4,5-c]-pyridine compounds which are substituted in positions corresponding to R^1, R^3, -X-Y-A-Z of the presently claimed compounds of formula (I). The compounds disclosed by Arcari are limited to those compounds of formula I which correspond to -Y-A-Z equal to $-NH_2$, optionally substituted with C_{1-4}-alkyl, amino, cyano, nitro or acylamino.

No other compounds or functional groups are disclosed in Arcari. For example, the pending claims include as possible substituent for -Y-A-Z (in the case where -Y-A- is a valence bond):

> C_{1-6}-alkyl, C_{2-6}-alkenyl or C_{2-6}-alkynyl,
> aryl, C_{3-15}-cycloalkyl, C_{3-15}-cycloalkenyl, C_{3-15}-cycloalkynyl, aroyl, heteroaryl,
> $-NR^{13}R^{14}$, in which R^{13} and R^{14} are both phenyl, which phenyl groups are joined with a C_{1-4}-alkylene group to form a tricyclic ring system,
> $-CHR^{13}R^{14}$, in which R^{13} is C_{1-6}-alkyl or phenyl, and R^{14} is phenyl, or R^{13} and R^{14} are both C_{1-6}-alkyl which are joined with C_{1-4}-alkylene linkers to form a polycarbocyclic ring system, or
> $-CR^{13}R^{14}R^{15}$, in which R^{13}, R^{14} and R^{15} are C_{1-6}-alkyl which are joined with C_{1-4}-alkylene linkers to form a polycarbocyclic ring system.

None of these groups are disclosed by the Arcari reference, and there is not suggestion or motivation in the cited reference to consider these substitutions.

Accordingly, Arcari does not suggest any modification of the disclosed functional groups. Further, Arcari does not provide any motivation or suggestion to one skilled in the art to make any substitution on the imidazopyridine core that correspond to the R^2, R^4, R^5, R^6, or the other possible substitutions for R^1, R^3, and the -X-Y-A-Z group which are encompassed by the pending claims.

With respect to pharmacological activity, Arcari teaches that the compounds are useful for the suppression of stomach ulcers and the reduction of gastric acid secretions. (Arcari, page 8, lines 5 to 11.) Arcari provides no teaching or suggestion that the disclosed compounds would have any histamine H3 receptor activity. The presently claimed compounds are shown to possess a high and selective binging affinity for the histamine H3 receptor. As a result, the claimed compounds are useful for the treatment and/or prevention of diseases including obesity,

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[2] For a proper 35 USC 103 rejection, the reference must provide some suggestion, which would motivate the skilled artisan to modify the reference teaching as suggested by the Examiner. In re Fitch,

atheroscleosis, hypertension, impaired glucose tolerance, diabetes, dyslipidemia, coronary heart disease, gallbladder disease, osteoarthritis, certain types of cancer, diseases associated with the regulation of sleep, conditions associated with epilepsy, dementia and Alzheimer's disease.

There is no suggestion in Arcari that the modifications suggested by the Examiner to compounds disclosed therein would have any impact on the suppression of stomach ulcers or on the reduction of gastric acid secretion—the only pharmacological effect disclosed. Neither is there any suggestion or motivation in Arcari that the disclosed compounds, or any modifications thereof, would possess any activity related to the histamine H3 receptor of the claimed compounds.

Accordingly, the Arcari reference fails to provide the necessary incentive or motivation for modifying the reference in a manner that would produce the invention as claimed. For the foregoing reasons, Applicants submit that the amended claims overcome this rejection under 35 U.S.C. § 103 and respectfully request reconsideration and withdrawal of the rejection.

VIII. The Rejection of Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32, and 33-37 under 35 U.S.C. § 103

Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32, and 33-37 are rejected under 35 U.S.C. § 103 as being unpatentable in view of Scarponi et al., GB 2158440. Specifically, the Office Action states that the claimed invention differs from the reference by reciting a specific species and/or a more limited genus than the reference, and that it would have been obvious to one skilled in the art to be motivated to select any of the species of the genus taught by the reference because the skilled chemist would have a reasonable expectation that any species selected would have similar properties as the same use as taught for the genus as a whole. (Office Action, page 13). This rejection is respectfully traversed.

Applicants respectfully assert that the present invention is not rendered obvious by the cited reference. As discussed above with respect to the 35 U.S.C. § 102 rejection based on the Scarponi reference, the amended claims do not encompass any of the compounds disclosed in Scarponi. Contrary to the Examiner's statement, it is respectfully asserted that the compounds encompassed by the amended claims are not specific species included in the generic scope of the

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23 USPQ 2d 1730, 1783-84 (Fed. Cir. 1992).

compounds taught in the Scarponi reference. Further, the Scarponi reference does not include any suggestion or motivation to one skilled in the art to modify the compounds disclosed therein, to make and use the presently claimed compounds.

With respect to pharmacological activity, Scarponi teaches that the compounds are useful as antiviral agents. (Scarponi: Abstract; page 4, lines 3 to 32; Tables I, II, and III.) Scarponi provides no teaching or suggestion that the disclosed compounds would have any histamine H3 receptor activity. In contrast, the presently claimed compounds are shown to possess a high and selective binging affinity for the histamine H3 receptor.

Further, there is no suggestion in Scarponi that the modifications suggested by the Examiner to compounds disclosed therein would have any impact on their antiviral activity—the only pharmacological effect disclosed. Neither is there any suggestion or motivation in Scarponi that the disclosed compounds, or any modifications thereof, would possess any activity related to the histamine H3 receptor of the claimed compounds and be active in the treatment of disease associated with the histamine H3 receptor.

Accordingly, the Scarponi reference fails to provide the necessary incentive or motivation for modifying the reference in a manner that would produce the invention as claimed. For the foregoing reasons, Applicants submit that the amended claims overcome this rejection under 35 U.S.C. § 103 and respectfully request reconsideration and withdrawal of the rejection.

IX. The Rejection of Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32, and 33-37 under 35 U.S.C. § 103

Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32, and 33-37 are rejected under 35 U.S.C. 103 as being unpatentable in view of Honma et al., EP 0531874. Specifically, the Office Action states that the claimed invention differs from the reference by reciting a specific species and/or a more limited genus than the reference, and that it would have been obvious to one skilled in the art to be motivated to select any of the species of the genus taught by the reference because the skilled chemist would have a reasonable expectation that any species selected would have similar properties as the same use as taught for the genus as a whole. (Office Action, page 13-14.) This rejection is respectfully traversed.

Applicants respectfully assert that the present invention is not rendered obvious by the cited reference. It is respectfully asserted that the compounds encompassed by the amended claims are not specific species included in the generic scope of the compounds taught in the Honma reference.

The claims are amended herein to include the limitation that when R^2=hydrogen or lower alkyl, R^3=carboxyl or C_{1-6}-alkoxycarbonyl, R^4=R^5=R^6=hydrogen, -X- = -C(=O)- or -CH_2- and -Y-A-Z= hydrogen, or -R^9, wherein R^9 is optionally substituted C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{1-6}-alkylsulfonyl, amino or phenyl, R^1 must not be -CH_2-phenyl-phenyl. Accordingly, the amended claims do not encompass the compounds disclosed in Honma.

Contrary to the Examiner's statement, it is respectfully asserted that the compounds encompassed by the amended claims are not specific species included in the generic scope of the compounds taught in the Honma reference. Further, the Honma reference does not include any suggestion or motivation to one skilled in the art to modify the compounds disclosed therein, to make and use the presently claimed compounds.

With respect to pharmacological activity, Honma teaches that the compounds are useful as angiotensin II antagonists for the treatment of high blood pressure and central nervous system diseases. Honma provides no teaching or suggestion that the disclosed compounds would have any histamine H3 receptor activity. In contrast, the presently claimed compounds are shown to possess a high and selective binging affinity for the histamine H3 receptor.

Further, there is no suggestion in Honma that the modifications suggested by the Examiner to compounds disclosed therein would have any impact on their antiviral activity—the only pharmacological effect disclosed. Neither is there any suggestion or motivation in Honma that the disclosed compounds, or any modifications thereof, would possess any activity related to the histamine H3 receptor of the claimed compounds and be active in the treatment of disease associated with the histamine H3 receptor.

Accordingly, the Honma reference fails to provide the necessary incentive or motivation for modifying the reference in a manner that would produce the invention as claimed. For the foregoing reasons, Applicants submit that the amended claims overcome this rejection under 35 U.S.C. § 103 and respectfully request reconsideration and withdrawal of the rejection.

X. The Rejection of Claims 1-3, 5, 7-13, 15, 20-23, 25, 30, 32, and 33-37 under 35 U.S.C. § 103

Claims 1-3, 5, 7-13, 20-23, 25, 30, 32, and 33-37 are rejected under 35 U.S.C. § 103 as being unpatentable in view of Kureha et al., EP 0589665 (also referred to as Enari above). Specifically, the Office Action states that the claimed invention differs from the reference by reciting a specific species and/or a more limited genus than the reference, and that it would have been obvious to one skilled in the art to be motivated to select any of the species of the genus taught by the reference because the skilled chemist would have a reasonable expectation that any species selected would have similar properties as the same use as taught for the genus as a whole. (Office Action, page 14-15). This rejection is respectfully traversed.

Applicants respectfully assert that the present invention is not rendered obvious by the cited reference. As discussed above with respect to the 35 U.S.C. § 102 rejection based on the Enari reference, the amended claims do not encompass any of the compounds disclosed in Hureha. Contrary to the Examiner's statement, it is respectfully asserted that the compounds encompassed by the amended claims are not specific species included in the generic scope of the compounds taught in the Hureha reference. Further, the Hureha reference does not include any suggestion or motivation to one skilled in the art to modify the compounds disclosed therein, to make and use the presently claimed compounds.

With respect to pharmacological activity, Hureha teaches that the compounds are useful as angiotensin II antagonists for the treatment of high blood pressure and central nervous system diseases. Hureha provides no teaching or suggestion that the disclosed compounds would have any histamine H3 receptor activity. In contrast, the presently claimed compounds are shown to possess a high and selective binging affinity for the histamine H3 receptor.

Further, there is no suggestion in Hureha that the modifications suggested by the Examiner to compounds disclosed therein would have any impact on their antiviral activity—the only pharmacological effect disclosed. Neither is there any suggestion or motivation in Hureha that the disclosed compounds, or any modifications thereof, would possess any activity related to the histamine H3 receptor of the claimed compounds and be active in the treatment of disease associated with the histamine H3 receptor.

Accordingly, the Hureha reference fails to provide the necessary incentive or motivation

for modifying the reference in a manner that would produce the invention as claimed. For the foregoing reasons, Applicants submit that the amended claims overcome this rejection under 35 U.S.C. § 103 and respectfully request reconsideration and withdrawal of the rejection.

XI. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: November 1, 2001

Peter J. Waibel, Reg. No. 43,228
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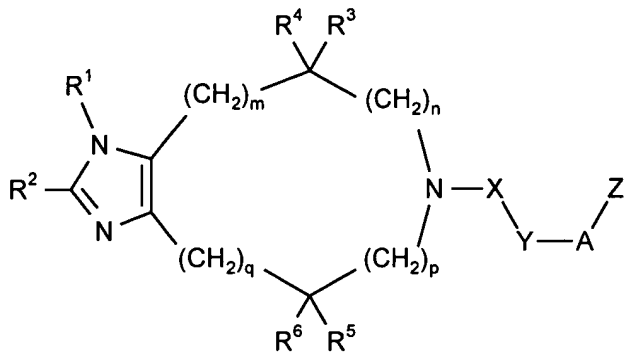
VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A compound of formula **I**



I

wherein

R^1 is hydrogen or a functional group, which can be converted to hydrogen *in vivo*;

R^2 is hydrogen, C_{1-6}-alkyl, halogen, cyano, trifluoromethyl, trifluoromethoxy, hydroxy or $-NR^7R^8$,

wherein R^7 and R^8 independently are

hydrogen,

C_{1-6}-alkyl optionally substituted with

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino, heteroarylamino or C_{3-8}-cycloalkyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl or heteroarylsulfonyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

C_{1-6}-alkylsulfonyl optionally substituted with

C_{3-8}-cycloalkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino, or

R^7 and R^8, together with the nitrogen atom to which they are connected, form a 3 to 8-membered, saturated or unsaturated, heterocyclic ring optionally containing one or more further heteroatoms selected from nitrogen, oxygen and sulfur, and optionally substituted with C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino;

R^3, R^4, R^5 and R^6 independently are hydrogen, carboxy, C_{1-6}-alkoxycarbonyl, cyano, trifluoromethyl, halogen,

C_{3-8}-cycloalkyl optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)-amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

C_{1-6}-alkyl, C_{2-6}-alkenyl or C_{2-6}-alkynyl, which are optionally substituted with

C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, cyano, halogen, trifluoromethyl, trifluoromethoxy, carboxy, C_{1-6}-alkoxycarbonyl,

C_{3-8}-cycloalkyl, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino, heteroarylamino or -CO-NR^9R^{10},

aryl optionally substituted with

halogen, cyano, nitro, C_{1-6}-alkyl, C_{1-6}-alkoxy, hydroxy, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aryloxy, aroyl, heteroaroyl, arylsulfonyl, arylamino, heteroarylamino or -CO-NR^9R^{10},

-CO-NR^9R^{10},

wherein R^9 and R^{10} independently are

hydrogen,

C_{1-6}-alkyl optionally substituted with

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino, heteroarylamino or C_{3-8}-cycloalkyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl or heteroarylsulfonyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

C_{1-6}-alkylsulfonyl optionally substituted with

C_{3-8}-cycloalkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino, or

R^9 and R^{10}, together with the nitrogen atom to which they are connected, form a 3 to 8 membered, saturated or unsaturated, heterocyclic ring optionally containing one or more further heteroatoms selected from nitrogen, oxygen and sulfur, and optionally substituted with C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino, or

R^3 and R^4, together with the carbon atom to which they are connected, and/or R^5 and R^6 together with the carbon atom to which they are connected, form a 3 to 8-membered, saturated or unsaturated, carbocyclic or heterocyclic ring optionally substituted with C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino;

[m, n, p and q independently are 0, 1 or 2]

m, n, p are 0, and q is 1;

X is a valence bond, $-CH_2-$, $-C(=O)-$, $-C(=S)-$, $-S(=O)-$, $-S(=O)_2-$, $-C(=N-CN)-$, $-C(=CH-NO_2)-$, $-C(=C(CN)_2)-$, $-C(=CH-CN)-$, $-C(=NR^{11})-$ or $-C(=N-S(=O)_2R^{11a})-$, wherein R^{11} is

hydrogen,

C_{1-6}-alkyl optionally substituted with

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino, heteroarylamino or C_{3-8}-cycloalkyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl or heteroarylsulfonyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

C_{1-6}-alkylsulfonyl optionally substituted with

C_{3-8}-cycloalkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino;

R^{11a} is C_{1-6}-alkyl optionally substituted with

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino, heteroarylamino or C_{3-8}-cycloalkyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl or heteroarylsulfonyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

Y is a valence bond, -O- or -N(R^{12})-,

wherein R^{12} is

hydrogen,

C_{1-6}-alkyl optionally substituted with

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino, heteroarylamino or C_{3-8}-cycloalkyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl or heteroarylsulfonyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

C_{1-6}-alkylsulfonyl optionally substituted with

C_{3-8}-cycloalkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino;

A is a valence bond, C_{1-8}-alkylene, C_{2-8}-alkenylene, C_{2-8}-alkynylene, C_{3-8}-cycloalkylene or phenylene, or

when Y is -N(R^{12})-, A, together with R^{12} and the nitrogen atom to which they are connected, may form a 3 to 8-membered, saturated or unsaturated, heterocyclic ring system optionally containing one or more further heteroatoms selected from nitrogen, oxygen and sulfur, and optionally substituted with C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl,

trifluoromethoxy, aryl, heteroaryl, aryl-C_{1-6}-alkyl, heteroaryl-C_{1-6}-alkyl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino; and

Z is [-R^{13}, -OR^{13}, -SR^{13}, -$NR^{13}R^{14}$, -$CHR^{13}R^{14}$, -$CR^{13}R^{14}R^{15}$ or =$CR^{13}R^{14}$,

wherein R^{13}, R^{14} and R^{15} independently are

hydrogen,]

C_{1-6}-alkyl, C_{2-6}-alkenyl or C_{2-6}-alkynyl, which are optionally substituted with

aryl, arylamino, heteroarylamino, aroyl, heteroaroyl, arylsulfonyl, C_{1-6}-alkylsulfonyl, sulfonylamino, arylthio, heteroarylthio, aryloxy, acylamino, heteroaryl or C_{3-8}-cycloalkyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, aryl-C_{1-6}-alkyl, heteroaryl-C_{1-6}-alkyl, nitro, arylamino, heteroarylamino, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, C_{1-6}-alkylsulfonyl, sulfonylamino, arylthio, heteroarylthio, aryloxy, acylamino, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethoxy or trifluoromethyl,

aryl, C_{3-15}-cycloalkyl, C_{3-15}-cycloalkenyl, C_{3-15}-cycloalkynyl, aroyl or heteroaryl, which are optionally substituted with

aryl-C_{1-6}-alkyl, heteroaryl-C_{1-6}-alkyl, aryl, heteroaryl, nitro, arylamino, heteroarylamino, aroyl, heteroaroyl, arylsulfonyl, heteroarylsulfonyl, C_{1-6}-alkylsulfonyl, sulfonylamino, arylthio, heteroarylthio, aryloxy, acylamino, C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, C_{3-8}-cycloalkanecarbonyl, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethoxy or trifluoromethyl, [where

R^{13} and R^{14} or R^{13}, R^{14} and R^{15}, when they do not represent hydrogen, may be joined by one or more bridging linkers such as a valence bond, C_{1-4}-alkylene, C_{2-4}-alkenylene, -O-, -S-, -N(R^{16})-, -C(=O)-, -S(=O)-, -S(=O)$_2$-, -C($R^{16}R^{17}$)-, phenylene, biphenylene, -O-C_{1-4}-alkylene, -S-C_{1-4}-alkylene, -N(R^{16})-C_{1-4}-alkylene, -N=C_{1-4}-alkylene, -O-C_{2-4}-alkenylene, -S-C_{2-4}-alkenylene or -N(R^{16})-C_{2-4}-alkenylene, to form a mono-, bi- or polycyclic ring system,

wherein R^{16} and R^{17} independently are

hydrogen,

C_{1-6}-alkyl optionally substituted with

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino, heteroarylamino or C_{3-8}-cycloalkyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl or heteroarylsulfonyl, which are optionally substituted with

C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino,

C_{1-6}-alkylsulfonyl optionally substituted with

C_{3-8}-cycloalkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino, or

R^{16} and R^{17}, together with the nitrogen atom to which they are connected, form a 3 to 8 membered, saturated or unsaturated, heterocyclic ring optionally containing one or more further heteroatoms selected from nitrogen, oxygen and sulfur, and optionally substituted with C_{1-6}-alkyl, C_{1-6}-alkoxy, C_{1-6}-alkylthio, hydroxy, amino, C_{1-6}-alkylamino, di(C_{1-6}-alkyl)amino, halogen, cyano, trifluoromethyl, trifluoromethoxy, aryl, heteroaryl, aroyl, heteroaroyl, arylsulfonyl, arylamino or heteroarylamino;]

-$NR^{13}R^{14}$, in which R^{13} and R^{14} are both phenyl, which phenyl groups are joined with a C_{1-4}-alkylene group to form a tricyclic ring system,

-$CHR^{13}R^{14}$, in which R^{13} is C_{1-6}-alkyl or phenyl, and R^{14} is phenyl, or R^{13} and R^{14} are both C_{1-6}-alkyl which are joined with C_{1-4}-alkylene linkers to form a polycarbocyclic ring system, or

-$CR^{13}R^{14}R^{15}$, in which R^{13}, R^{14} and R^{15} are C_{1-6}-alkyl which are joined with C_{1-4}-alkylene linkers to form a polycarbocyclic ring system,

wherein

heteroaryl is a 3 to 7 membered monocyclic or a 9 to 14 membered bi- or tricyclic aromatic system containing one or more heteroatoms selected from N, O or S, which is optionally partially or fully hydrogenated;

heteroarylamino is a radical wherein a -(NH)- group is linked to a heteroaryl group;

heteroaroyl is a radical wherein a -(C=O)- group is linked to a heteroaryl group;

provided that

when X is -CS-, $R^1=R^2=R^5=R^6$=hydrogen, [m=n=p=0 and q=1,] the group -Y-A-Z must not start with the radical -NH-;

when the group -X-Y-A-Z starts with the radical -CH_2-, $R^1=R^2=R^6$=hydrogen, [m=n=p=0 and q=1,] R^5 must not be carboxy or aminocarbonyl;

when X is -CO-, the group -Y-A-Z starts with the radical -NH-, $R^1=R^2=R^6$=hydrogen, [m=n=p=0 and q=1,] the remainder of the group -Y-A-Z must not be hydrogen, unsubstituted or C_{1-6}-alkoxy substituted phenyl, unsubstituted C_{3-8}-cycloalkyl or unsubstituted C_{1-6}-alkyl;

when X is -CO-, Y is -O-, A is -CH_2-, Z is phenyl, $R^1=R^2=R^3=R^4=R^6$=hydrogen, [m=n=p=0 and q=1,] R^5 must not be carboxy, aminocarbonyl or 4-phenylpiperazin-1-ylcarbonyl;

when X is -CO-, Y is -O-, A is -CH_2-, Z is phenyl, $R^1=R^3=R^4=R^6$=hydrogen, R^2=butyl, [m=n=p=0 and q=1,] R^5 must not be methoxycarbonyl;

when X is -CO-, Y is -O-, A is -CH_2-, Z is phenyl, $R^1=R^2=R^4=R^5=R^6$=hydrogen, [m=n=p=0 and q=1,] R^3 must not be hydrogen, ethyl, isopropyl or phenyl;

when X is -CO-, Y is -O-, A is a valence bond, Z is *tert*-butyl, $R^1=R^2=R^3=R^4=R^6$=hydrogen, [m=n=p=0 and q=1,] R^5 must not be carboxy;

when X is -CO-, Y is -O-, A is a valence bond, Z is *tert*-butyl, $R^1=R^2=R^4=R^5=R^6$=hydrogen, [m=n=p=0 and q=1,] R^3 must not be 4-cyanophenyl;

when X is -CO-, the group -Y-A-Z starts with the radical -O-, $R^1=R^2=R^6$=hydrogen, [m=n=p=0 and q=1,] R^5 must not be carboxy, aminocarbonyl or hydrogen;

when -X is -CO-, the group -Y-A-Z starts with the radical -CH<, $R^1=R^2=R^3=R^4=R^6$=hydrogen, [m=n=p=0 and q=1,] R^5 must not be hydroxymethyl, C_{1-6}-alkoxycarbonyl or carboxy; [and]

when X is -CO-, the group -Y-A-Z is 4-methoxyphenyl, $R^1=R^2=R^3=R^4=R^6$=hydrogen, [m=n=p=0 and q=1,] R^5 must not be carboxy;

when $R^1=R^2=R^3=R^4=R^5=R^6$=hydrogen, -X-Y-A-Z must not be methyl;

when $R^1=R^2=R^3=R^4$=hydrogen, C_{1-4}-alkyl, C_{2-4}-alkeny or phenyl, or $R^2=R^3=R^4=C_{3-7}$-cycloalkyl, R^6=hydrogen, and XYAZ begins with -C(=O)-, -C(=O)-O-, -C(=O)-NH- or -C(=S)-NH-, R^5 must not be -C(=O)-NH_2, which is optionally substituted with C_{1-4}-alkyl, C_{2-4}-alkenyl, C_{3-7}-cycloalkyl, or phenyl;

when $R^1=R^2=R^4=R^5=R^6$=hydrogen, and R^3 = 4-methylphenyl, 4-methoxyphenyl or 4-chlorophenyl, -X-Y-A-Z must not be methyl, -CH_2-phenyl or benzoyl;

when $R^1=R^2=R^3=R^4=R^5=R^6$=hydrogen, -X-Y-A-Z must not be 2-methoxy-4-amino-5-chloro benzoyl;

when $R^1=R^2=R^3=R^4=R^5$=hydrogen, and R^6=carboxy, -X-Y-A-Z must not be (4-methoxyphenyl)sulfonyl; and

when R^2=hydrogen or lower alkyl, R^3=carboxyl or C_{1-6}-alkoxycarbonyl, $R^4=R^5=R^6$=hydrogen, -X- = -C(=O)- or -CH_2- and -Y-A-Z= hydrogen, or -R^9 wherein R^9 is optionally substituted C_{1-6}-alkyl, C_{2-6}-alkenyl, C_{1-6}-alkylsulfonyl, amino or phenyl, R^1 must not be -CH_2-phenyl-phenyl;

[as well as] or any optical or geometric isomer or tautomeric form thereof or a pharmaceutically acceptable salt thereof.

14. (Amended) A compound of claim [17] 12, wherein Z is phenyl or cyclohexyl which are optionally substituted as defined in claim 1.

46. (Amended) A method of treating or preventing overweight or obesity comprising administering to a subject in need thereof a pharmaceutical composition of claim [40] 34.

48. (Amended) A method of treating or preventing disorders and diseases related to overweight or obesity comprising administering to a subject in need thereof a pharmaceutical composition of claim [40] 34.